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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/563,031 | 03/07/2006 | Maria Jose Alonso Fernandez | 4258-117 | 6063 |

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INTELLECTUAL PROPERTY / TECHNOLOGY LAW
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| EXAMINER | |
|---|---|
| WESTERBERG, NISSA M | |

| ART UNIT | PAPER NUMBER |
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| 1618 | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/563,031 | FERNANDEZ ET AL. | |
| | Examiner | Art Unit | |
| | Nissa M. Westerberg | 1618 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *28 July 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1 - 17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 - 17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

**DETAILED ACTION**

Applicants' arguments, filed July 28, 2008, have been fully considered but they are not deemed to be fully persuasive. The following rejections and/or objections constitute the complete set presently being applied to the instant application.

***Claim Rejections - 35 USC § 102***

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. Claims 1, 2, 3, 6, 7 and 10 – 17 were rejected under 35 U.S.C. 102(b) as being anticipated by Grandfils et al. (US 5,962,566). This rejection is MAINTAINED for the reasons of record set forth in the Office Action mailed March 27, 2008 and those set forth below. Due to the amendments to the claims, this rejection is applied to claims 12 – 17.

Applicant traverses this rejection on the basis that the amended claims now require the use of a non-polar organic solvent which contains both the biodegradable polymer and POE-containing polymer which is added with stirring to a polar phase. Grandfils et al. does not disclose or suggest using a non-polar solvent to dissolve the

polymers just prior to their mixture with the aqueous phase and requires a solvent evaporation step. Additionally, the compositions of Grandfils et al. contains cholesterol, a surfactant, which if not added, results in the formation of microparticles. As the process is patentable, the "product produced by the product is also patentable" (p 7 of the response).

These arguments are not found to be fully persuasive. Due to the amendments to the claims, the rejection under 35 USC 102(b) over the method of making the particles is withdrawn but the rejection is maintained over the product and product-by-process claims. If a product is found to be novel, then the process to make that product is also novel. However, a process to make a product when claimed in the product-by-process format must result in a different, non-obvious product in order for the product by process claims. "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985) (citations omitted) **MPEP 2113**. Applicant has not presented any evidence that a nanoparticle produced using a non-polar organic solvent in place or polar organic solvent results in the production of such a product.

While the nanoparticles of the prior art contain cholesterol, this ingredient is not excluded from the nanoparticles of the instant claims as the claims use the open

language of "comprising". The Examiner was also unable to locate a passage in Grandfils et al. relating to result achieved in compositions that did not include cholesterol. The Applicant is kindly requested to point by column and line number to where support may be found in this document, or by the submission of evidence such as in the form of a declaration, for this information.

***New Claim Rejections - 35 USC § 103***

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein

were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 1 – 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Grandfils (US 5,962,566) in view of Levy et al. (WO 96/20698).

The teachings of Grandfils et al. have been discussed in the Office Action mailed March 27, 2008 and above. In the process of making the nanoparticles disclosed by Grandfils et al., a biodegradable polymer and polyoxyethylene-derived block copolymer are dissolved in a polar organic solvent, which is dried, cholesterol is added and that is dissolved in the polar organic solvent DMSO prior to mixing with the polar phase which results in nanoparticle formation (e.g., example 1 in col 5)

Grandfils et al. does not disclose a process for making nanoparticle in which the polymer components are dissolved in a non-polar organic solvent which is mixed with the polar phrase, resulting in the formation of nanoparticles. Grandfils et al. also does not disclose the use of polyanhydrides or poloxamines in the nanoparticles.

Levy et al. discloses biodegradable controlled release nanoparticles (abstract). When hydrophilic active agents are to be incorporated into the nanoparticles, the polymer is dissolved in a nonpolar organic solvent such as methylene chloride or chloroform (p 18, ln 8 – 11). The bioactive agent is dissolved in a semipolar organic

solvent which, after being combined with the nonpolar organic solvent, is emulsified with an aqueous phase to form nanoparticles (p 18, ln 11 – 15). In example 1 (p 30), the polymer and drug are dissolved in methylene chloride and added directly to the aqueous phase (p 30, ln 18 – p 31, ln 4). Among the biocompatible, biodegradable synthetic polymers which may be used to form nanoparticles are polyanhydrides (p 7, ln 17 – 20). Poloxamers such as those sold under the trade name TETRONIC® 908 can be included as a synthetic polymer which is useful for modifying the surface of the particles (p 13, ln 10 – 15). These surface agents allow for targeting, enhanced sustained drug release, protection of the bioactive ingredient improve suspendability and/or preventing aggregation of the nanoparticles (p 13, ln 1 – 7).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to take the teachings of Levy et al. which do not require both a polar and nonpolar organic solvent solution in order to produce nanoparticles and to simply use the polymer dissolved in a nonpolar aqueous solvent added, with stirring, to a polar phase to generate nanoparticles, as taught by Grandfils et al. The polarity and final choice of solvent used to make the nanoparticles is dependent on a number of factors, including the solubility of the polymers being used as well as the polarity of the active ingredient being incorporated in the nanoparticles. One of ordinary skill in the art particularly in view of the teachings of Levy et al. would be aware that the polymers dissolved in a nonpolar organic solvent need not be evaporated and resuspended in a polar organic solvent in order for nanoparticles to be produced when the organic solution is mixed with a polar phase.

Polyanhydrides are taught by Levy et al. as biocompatible and biodegradable materials which are functionally equivalent to those taught as suitable for nanoparticle formation by Grandfils et al. (see col 2, ln 28 – 35). It also would have been obvious to one of ordinary skill in the art to include a poloxamine in the nanoparticle composition of Grandfils et al., taught by Levy et al. to improve a variety of features of the nanoparticles, such as preventing aggregation of particles, allow for targeting or enhance drug release from the nanoparticles.

***Conclusion***

7. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nissa M. Westerberg whose telephone number is (571)270-3532. The examiner can normally be reached on M - F, 8:00 a.m. - 4 p.m. ET.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael G. Hartley/
Supervisory Patent Examiner, Art Unit 1618

NMW